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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Apollon Papadimitriou

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
340 KINGSLAND STREET
NUTLEY, NJ 07110

EXAMINER

KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 12/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/853,731	Applicant(s) PAPADIMITRIOU, APOLLON	
	Examiner Chih-Min Kam	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24, 25, 27-34, 38-42, 51-55, 59-61, 67, 68, 71-77 and 83-108 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 24, 25, 27-34, 38-42, 51-55, 59-61, 87 and 90 is/are allowed.
- 6) ☒ Claim(s) 67, 68, 71, 73, 75, 77, 83-86, 88, 89, 91-101, 104 and 106 is/are rejected.
- 7) ☒ Claim(s) 72, 74, 76, 102, 103, 105, 107 and 108 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. Claims 24, 25, 27-34, 38-42, 51-55, 59-61, 67, 68, 71-77 and 83-108 are pending.

Applicants' amendment filed on September 23, 2005 is acknowledged. Applicants' response has been fully considered. Claims 67 and 73 have been amended. Thus, claims 24, 25, 27-34, 38-42, 51-55, 59-61, 67, 68, 71-77 and 83-108 are examined.

Withdrawn Claim Rejections-Obviousness Type Double Patenting

2. The previous rejection of claims 67-68, 71, 73, 75, 77, 83, 85, 86, 91-101 and 104 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U. S. Patent 6,583,272, is withdrawn in view of applicant's submission of a terminal disclaimer, and applicant's response at page 15 of the amendment filed September 23, 2005.

3. The previous rejection of claims 67-68, 71-77 and 91-108 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U. S. Patent copending Application No. 10/014,363, is withdrawn in view of claims 1-16 in the Application No. 10/014,363 being cancelled in the amendment filed November 25, 2005, and applicant's response in the amendment filed September 23, 2005.

4. The previous rejection of claims 24, 25, 27-34, 38-42, 51-55, 59-61, 67, 68, 71-77 and 83-108 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16, 18, 22-37 and 39-68 of U. S. Patent copending Application No. 10/780,297 (available as US 2004/0147431; allowable claims), is withdrawn in view of

Art Unit: 1656

applicant's submission of a terminal disclaimer, and applicant's response at page 16 in the amendment filed September 23, 2005.

Maintained Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 83, 84, 88 and 89 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 83, 84, 88 and 89 are indefinite as to a pharmaceutical composition containing an EPO product, arginine and sodium sulfate with a pH at 6 to 6.5 or pH 6.2, since arginine has a pKa of 1.8, 9 and 12.5, and H₂SO₄ is a strong acid, it is not clear how the pH of the composition is maintained at pH about 6-6.5 without including a buffer reagent having a pKa in the range of pH 5 to 7.5.

Response to Arguments

Applicants indicate the claims are directed to liquid pharmaceutical compositions comprising a minimum of certain components, namely, an erythropoietin glycoprotein, sodium sulfate and arginine, and having a particular pH (from about 6 to about 6.5). As the claims contain the term "comprising," it is not legally required that the pH range be achieved with just the enumerated components. On the contrary, the claimed compositions may include other components, for example as is shown in the Examples. The pH range is a required parameter of the claims, it is not necessarily a direct result of just the specifically-enumerated components of the compositions of the claims (page 14 of the response).

Art Unit: 1656

Applicants' response has been fully considered, however, the argument is not found persuasive because the claims cite the composition comprising erythropoietin, sodium sulfate and arginine and having a pH of from about 6 to about 6.5, while the cited components do not provide the particular pH of the composition, and the composition needs to maintain at pH 6 to 6.5 and to be stable at room temperature, it is not clear what components are needed for the composition to maintain at pH 6.2-6.5.

Maintained Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Previous rejection of claims 67-68, 71, 73, 75, 77, 83, 85, 86, 91-101 and 104 under 35 U.S.C. 102(e) as being anticipated by Bailon (U.S. Patent 6,583,272 B1, priority date July 2, 1999) is maintained, and claim 106 is added to the rejection. Response to applicant's argument is shown below.

Art Unit: 1656

Bailon teaches a conjugate of erythropoietin (EPO) with poly(ethylene glycol) (PEG) and a pharmaceutical composition comprising therapeutically effective amount of the conjugate for administering to patients (column 3, lines 23-46), wherein the conjugate comprises an EPO such as human EPO and analogs having at least one free amino group and having in vivo biological activity. The EPO conjugate can be represented by formula (I), $P-[NHCO-(CH_2)_x-(OCH_2CH_2)_m-OR]_n$, wherein R is lower alkyl, x is 2 or 3, m is 450-900, n is 1-3, n and m are such that the molecular weight of the conjugate minus the EPO is from 20 to 100 kDa (column 1, line 64-column 3, line 6; column 3, line 48-column 4, line 31) and the EPO including both naturally or recombinantly produced human erythropoietin having the amino acid sequence of SEQ ID NO:1 or 2 can be modified as analogs having 1-6 additional glycosylation sites or a rearrangement of at least one site for glycosylation, for example, the conjugate such as mono-PEG-EPO or di-PEG-EPO is prepared in a phosphate buffer, pH 7.5 with a 30 kDa methoxy PEG-SBA reagent (Examples 2, 5), and a pegylated EPO (10-400 $\mu\text{g/ml}$, Table 3; 0.6-1.2 mg/ml, Example 6) is formulated in a sulfate-containing buffer at pH 6.2, e.g., 10 mM phosphate, 140 mM sulfate, pH 6.2; 10 mM (corresponding to 1.38 mg/ml) phosphate, 40 mM (corresponding to 5.67 mg/ml) sulfate, 4% mannitol, pH 6.2; 50 mM arginine, 100 mM sulfate, pH 6.2 and these pegylated EPO in various formulations are stable at room temperature (Fig. 4; Example 8, Table 3; claims 67, 68, 71, 73, 75, 77, 83, 85, 86, 91-101, 104 and 106).

Response to Arguments

Applicants indicate the Declaration of Dr. Papadimitriou under 37 CFR 1.132 has been submitted on February 5, 2004, and in the Declaration, Dr. Papadimitriou averred that he is the sole inventor of formulations A-I presented in Example 8, Table 3 of U.S. Patent 6,583,272 by

Art Unit: 1656

Bailon; MPEP Section 715.01 provides that a Rule 132 Declaration may be used to overcome a Section 102(e) rejection "by proving that the subject matter relied upon in the reference or activity was applicant's own invention." Moreover, in Section 716.10, entitled "Attribution," an analogous fact pattern is indicated. Section 716.10 provides that an earlier filed application (in this case the Bailon patent) containing a disclosure that is not claimed and having an inventive entity that is different from a subsequently filed application claiming the earlier disclosed but not claimed subject matter is available as a reference against the subsequently filed application unless it is overcome by a Rule 131 declaration showing prior invention or a Rule 132 declaration stating the named inventor of the subsequent application "conceived or invented the subject matter disclosed in the (earlier) patent or published application. Disclaimer by the other patentee or other applicant of the published application should not be required but if submitted, may be accepted by the Examiner." MPEP § 716.10, pp. 700-249 to 250. Therefore, the Papadimitriou Declaration should be accepted and the rejection under 102(e) should be withdrawn (pages 17-18 of the response).

Applicants' response has been fully considered, however, the argument is not found persuasive because US Patent 6,583,272, which discloses the claimed EPO formulations, has only one inventor (i.e., Pascal Sebastian Bailon), while Dr. Papadimitriou is the sole inventor of instant application. Thus, the rejection under 35 USC 102(e) is proper. Furthermore, MPEP 715.01(a) provides that a Rule 132 Declaration may be used to overcome a Section 102(e) rejection under condition such that when subject matter, disclosed but not claimed in a patent or application publication filed jointly by S and another, is claimed in a later application filed by S, the joint patent or application publication is a valid reference unless overcome by affidavit or

Art Unit: 1656

declaration under 37 CFR 1.131 or an unequivocal declaration under 37 CFR 1.132 by S that he/she conceived or invented the subject matter disclosed in the patent or application publication. Moreover, Section 716.10 also provides that a Rule 132 Declaration may be submitted to overcome a Section 102(e) rejection under condition such that when subject matter, disclosed but not claimed in a patent or application publication filed jointly by S and another, is claimed in a later application filed by S, the joint patent or application publication is a valid reference unless overcome by affidavit or declaration under 37 CFR 1.131 showing prior invention or an unequivocal declaration under 37 CFR 1.132 by S that he/she conceived or invented the subject matter disclosed in the patent or application publication. However, in the instance case, Dr. Papadimitriou is not a joint inventor of the 6,583,272 patent, and Pascal Sebastian Bailon is not a joint invent of the instant application, thus the condition for filing an affidavit or a declaration under 37 CFR 1.131 showing prior invention or an unequivocal declaration under 37 CFR 1.132 to overcome 102 (e) rejection has not been met. Therefore, the declaration of Dr. Papadimitriou filed under 37 CFR 1.132 is not accepted to overcome the rejection under 102(e).

Claim Objections

7. Claims 72, 74, 76, 102, 103, 105, 107 and 108 are objected to because the claims are dependent from a rejected claim.

Art Unit: 1656

Conclusion

8. Claims 67-68, 71, 73, 75, 77, 83-86, 88, 89, 91-101, 104 and 106 are rejected, and claims 72, 74, 76, 102, 103, 105, 107 and 108 are objected to. It appears that claims 24, 25, 27-34, 38-42, 51-55, 59-61, 87 and 90 are free of art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner



**CHIH-MIN KAM
PATENT EXAMINER**

CMK

December 17, 2005